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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,132	REEVES ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2003 and 18 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 23, 2004 has been entered.

2. The amendment filed 10/18/04 does not include the correct status identifiers for each of the recited claims. Claims 32-68 are not "New" since the claims were presented in the response of January 1, 2004. Claims that were previously presented, but have not been amended should include the status identifier "previously presented." Claims that are in fact amended should include the status identifier "currently amended" and the amended text should be indicated by bracketing text to be deleted and underlining text that is to be added. For instance, claim 35, should be accompanied by the status identifier "currently amended" and the text "34" should be underlined, while the previously presented text of "3" should be bracketed. Further, claim 39, for example, includes underlining throughout the claim. However, the underlining does not correspond to the text that has been amended. All future amendments must comply with the revised amendment practice set forth in 37 CRF 1.121.

Election/Restrictions

3. This application contains claims directed to subject matter nonelected with traverse in Paper No. April 8, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

It is noted that the claims have been examined only to the extent that the claims read on SEQ ID NO: 13 and methods and compositions that require SEQ ID NO: 13 in combination with either SEQ ID NO: 56 or SEQ ID NO: 57. In claims that recite the additional subject matter of the sequences of SEQ ID NO: 1-12, 14-55, and 58-68, this subject matter has been withdrawn from consideration. FOR EXAMPLE, claim 35 has been examined only to the extent that the claim reads on SEQ ID NO: 13 in combination with SEQ ID NO: 56 or 57; claims 41 and 55 have been examined only to the extent that the claim reads on methods which require the use of SEQ ID NO: 13 in combination with SEQ ID NO: 57. In the claims that recite SEQ ID NO: 2, these claims have been examined only to the extent that the claims read on those portions of SEQ ID NO: 2 that include the sequences of SEQ ID NO: 56.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids consisting of SEQ ID NO: 1-68 and primers consisting of 10 to 20 nucleotide fragments of SEQ ID NO: 1 to 68 or consisting

of the sequence of the specific nucleotide positions of SEQ ID NO: 56 of nucleotides 79-861, 2011-2757, 5257-6471, 13156-13821, 2744-4135 and 858-2042 of SEQ ID NO: 56 and methods of detecting *E. coli* using said nucleic acids as probes and primers, does not reasonably provide enablement for any nucleic acid comprising SEQ ID NO: 13, 56 or 57 or comprising a part of SEQ ID NO: 13, 56 or 57. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn broadly to include nucleic acids comprising SEQ ID NO: 13, 56 or 57 or comprising a part of SEQ ID NO: 13, and compositions and methods requiring the use of a nucleic acid comprising SEQ ID NO: 13, 56, or 57 or comprising a part of SEQ ID NO: 13, 56 or 57. The specification does not provide a definition for the phrase "consisting essentially of" as it relates to a nucleic acid sequence and thereby this phrase has been interpreted to include nucleic acids containing SEQ ID NO: 13 and any additional flanking nucleotides. In view of the "comprising" and "part thereof" language, the claims encompass nucleic acids that include SEQ ID NO: 13, 56 or 57 and unspecified flanking nucleotides and nucleic acids containing an unspecified fragment of SEQ ID NO: 13, 56 or 57 of any length (1, 2, 3 etc nucleotides) flanked by nucleotides of undefined identity and length. The claims nucleic acids and compositions containing the nucleic acids are not defined in terms of any functional activity.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without □undue experimentation.□□ *In re Wright* 990 F.2d 1557, 1561. *In re*

Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement." In the instant case, the specification has not taught a representative number of nucleic acids within the claimed genus and has not provided sufficient guidance as to how to obtain additional nucleic acids without undue experimentation. The specification teaches isolated nucleic acids consisting of SEQ ID NO: 1-68, wherein the nucleic acids encode a flagellin protein from one of the E. coli strains of H1, 2, 4-7, 9-12, 14-16, 18-21, 23-2, 26-34, 38, 39, 41-43, 45, 46, 49, 51, 52 and 56. The specification teaches comparing the sequences of SEQ ID NO: 1-68 to one another in order to identify sequences that are specific for a given H serotype. However, the specification (page 2) also teaches that there are 4 loci in E. coli which encode for flagellin proteins, namely flk, fl1, flm, and fliC. The specification teaches that it is not clear as to which loci some of the presently claimed nucleic acids have been obtained from. It is stated that "we have used the term "flagellin gene" in many cases where previously one would have used "fliC" to allow for the uncertainty as to the locus introduced by recent observations" (see page 13). The specification asserts that most E. coli strains express a single H antigen and thereby it is the nucleic acid molecule itself that is important and not the source of the nucleic acid. Regardless of the fact that most E. coli strains only express one flagellin gene, it

appears that all E. coli strains contain each of the 4 flagellin loci. Yet, the specification has taught a single nucleic acid from each of the stated H types. The claims encompass nucleic acids from each of the loci of flk, fl1, flm and fliC from the 54 known H types of E. coli. While it is unclear as to which loci have been taught by the specification, it is clear that the specification has not taught a representative number of nucleic acids from each of the loci in each of the possible serotypes of E. coli. Furthermore, the specification demonstrates the unpredictability in obtaining the full length sequence of each of the flagellin genes in different E. coli H types. For example, at page 23, the specification states: "(f)or other strains, we were only able to amplify the flagellin gene using one or more of the other three pairs of primers, which are based on sequences within the *fliC* gene, and thus only partial sequence was obtained. These amplicons may be of the *fliC* gene or one of the alternative genes." At pages 26-28, the specification states that the full length flagellin genes from type strains H2, H3, H4, H5, H11, H17, H21, H24, H27, H29, H33, H38, H39, H42, and H56 have not been obtained. It is noted that the specification (page 24) states that the terminal regions of the flagellin gene are not important in determining antigenicity. However, the claims are inclusive of full length flagellin gene sequences which are not taught in the specification and the specification has established the unpredictability in obtaining these full length sequences. The specification (page 3) also teaches that the flagellin gene sequences for H8 and H40 were identical. Accordingly, these sequences cannot be used to determine the specific H serotype of E. coli but can only be used to determine whether the E. coli is type H8 or H40. Further, the specification (page 40) states that "(o)ur work

has shown that there are at least 7 cases where the H antigen type strains carry two antigen genes which appear to be complete and have the potential to function." The specification does not provide sufficient guidance as to how to obtain the flagellin genes from each of the 4 loci without undue experimentation. Further, the specification does not provide sufficient guidance as to how to distinguish between the nucleic acids from these loci and how to predictably identify subsequences within these as yet unisolated loci which are specific for an H serotype. As discussed by the specification the art of identifying and isolating the different flagellin genes from different loci is unpredictable. It is further unpredictable as to which sequences within these loci will be specific for a given H serotype. As taught in the specification (for example, page 31), some cross-reactivity with different strains is observed depending on the level of dilution of the anti-sera. For example, H11 cross reacts with anti-H21 and anti-H40. Accordingly, selection of subfragments of the flagellin gene that encode for type H specific antigens is unpredictable and can only be determined through experimentation. The claims also include SEQ ID NO: 9 which is characterized as being specific for H7 and SEQ ID NO: 14 which is specific for H12. It is unpredictable as to how these sequences which are specific for H1, H7 and H12 can also not encode a protein expressed by E. coli H1, H7 or H12. Additionally, the claims (for example, claims 33, 36, 41 etc) include nucleic acids which include only a portion of SEQ ID NO: 1-68.

The claims do not define the identity of the surrounding nucleotides and do not state the particular fragments of SEQ ID NO: 1-68 which would be required to provide the requisite attribute of allowing for the specific H serotype. For example, the

specification does not teach how to use a nucleic acid that includes 1, 10, or 20 nucleotides, etc. of SEQ ID NO: 13 flanked by nucleotides of any length and identity as a probe or primer. The claims thus include a very large genus of nucleic acids which are not adequately disclosed in the specification. Adequate guidance has not been provided in the specification as to how to predictably identify additional nucleic acids useful for determining the O serotype of E. coli without undue experimentation. Additionally, the steps recited in the method claims do not further define the structural or functional properties of the nucleic acids because the claims include detecting nucleic acids that hybridize to any degree and with any specificity to the claimed nucleic acid molecules under any conditions in order to detect any nucleic acid molecule that forms a hybrid with the claimed nucleic acids as a means "to detect the H and O serotype of the E. coli in the sample." Accordingly, in view of the lack of information in the specification as to how to reasonably identify other flagellin genes and genes useful for determining the O serotype of E. coli without undue experimentation and in view of the unpredictability in the art, the specification has not adequately taught one of skill in the art how to practice the claimed invention as it is broadly claimed.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33, 36-57, 59-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33 and 36 are indefinite and confusing. The claims depend from claims 32 and 34 which are drawn to nucleic acids comprising the nucleotide sequence of SEQ ID NO: 13. SEQ ID NO: 13 is 1368 nucleotides in length . However, claims 33 and 36 are inclusive of nucleic acids "according to claim 32" or "according to claim 34 or 35" which are 10-20 nucleotides in length. Claims 33 and 36 do not properly depend from claims 32 and 34 since the claims are not further limiting form claims 32 and 34. That is, claims 32 and 34 DO NOT include nucleic acids which are of a length of only 10-20 nucleotides. Thereby, it is unclear as to whether claims 33 and 36 are inclusive of any nucleic acid of 10-20 nucleotides, any nucleic acid of 10-20 nucleotides which includes a portion of SEQ ID NO: 13 or any nucleic acid comprising or consisting of 10-20 nucleotides of SEQ ID NO: 13.

In claim 33, the phrase "the molecules" lacks proper antecedent basis. While the claim previously refers to "a molecule" the claim does not previously refer to "molecules."

Claims 33 and 36 are indefinite over the recitation of "are from about 10 to 20 nucleotides in length" because it is not clear as to whether the claims are intended to be limited to molecules that consist of about 10 to 20 nucleotides or to molecules that are at least about 10 to 20 nucleotides in length (i.e., any molecule of a length greater than about 10 to 20 nucleotides).

Claim 36 is indefinite because it is unclear as to whether the phrase "the molecules" refers to the nucleic acid molecule consisting essentially of SEQ ID NO: 13

or the nucleic acid molecules comprising SEQ ID NO: 1-12 or 14-48 or to both of these nucleic acid molecules.

Claims 37-39, 57, and 66 are indefinite over the recitation of "corresponding " because this is not an art recognized term to describe the relationship between two nucleic acid sequences. It is not clear whether this refers to sequence homology/similarity or to sequence complementarity and it is not clear what percentage of homology or complementarity is encompassed by "corresponding" or under what types of conditions "corresponding" nucleotides are determined.

Claims 37-39, 41, 44, 45, 47, 48, 49, 56, 57, 62, 63 and 66 is indefinite over the recitation of "**a** nucleotide sequence" because it is not clear as to whether the claims intend to encompass primers that comprise the full length sequence set forth in the claims (e.g., in claim 39, a primer comprising nucleotides 892-909 of SEQ ID NO: 66) or if the claims intend to encompass primers that comprise a portion of the sequence set forth in the claims (e.g., in claim 39, a primer comprising 1, 2, 3 etc nucleotides 892-909 of SEQ ID NO: 66). That is, it is unclear as to whether "**a** nucleotide sequence of SEQ ID NO: _" refers to the full length sequence or a portion of the sequence.

Claims 39, 48, 52, 60, 61 are rejected as indefinite and confusing because the claims do not clearly set forth what constitutes the group from which the primers are selected. The claims include a table which lists "Positions of primer 1" and "Positions of primer 2". The position of a primer is distinct from the primer itself. Since the table does not specifically refer to individual primers, it is unclear as to what primer constitute the group of primers set forth in the tables. For example, with respect to claim 39, it is

unclear as to whether the primer consists of nucleotides 892-909 of SEQ ID NO: 66 or whether the primer is 100% complementary to nucleotides 892-909 of SEQ ID NO: 66 or whether the primer shares some level of complementarity and hybridizes to nucleotides 892-909 of SEQ ID NO: 66.

Claims 40-57, 59-67 are rejected as indefinite because the claims depend from a previously cancelled claims – see reference to cancelled claim 1 in present claims 40, 41, 43, 44, 46, 47, 50, 51, 54, 55, 59, and 67; reference to cancelled claims 3, 4, 6 and 8 in claim 57; reference to cancelled claim 6 in 66. Claims 40-65 and 67 have been interpreted as depending from claim 32, while claim 57 has been interpreted as depending from claim 34, 35, and 36 and claim 66 has been interpreted as depending from claim 37. However, in response to this Office action, Applicants are required to amend the claims to refer back to only currently pending claims.

Claims 40-56 and 62-65 are indefinite because it is unclear as to how the method steps accomplish the objective set forth in the claims. For instance, claim 40 is drawn to a method for detecting the H serotype of E. coli in a sample. This recitation infers that one distinguish between the serotypes of E. coli and that one determines the H serotype of E. coli in the sample, e.g. that one determines that a sample contains E. coli of serotype H1. However, the claims recite only a step of contacting a sample with a nucleic acid molecule under conditions that allow for hybridization with any nucleic acid molecule sharing any level of complementarity and detecting hybridization "to detect the serotype of the *E. coli* in the sample." The claims do not clarify how the step of detecting hybridization between nucleic acids sharing any level of complementarity results in

detecting the H serotype of E. coli in the sample. The recitation of "to detect the H serotype" does not clarify how the objective of detecting the H serotype of E. coli is accomplished. Additionally, the claims recite the step of "contacting a gene of an E. coli" with a nucleic acid molecule and then further recite a step that allows for hybridization of the molecule to a complementary nucleic acid molecule. The claims do not clarify the relationship between the gene and the complementary nucleic acid molecule.

Claims 43, 44, 50, 51, 52, 55 and 62-65 are indefinite over the recitation of "a pair of nucleic acid molecules according to claim 1 because this phrase lacks proper antecedent basis since claim 1 has been cancelled and independent claim 32 does not previously refer to a pair of nucleic acid molecules. Similarly, claims 50-53 are further indefinite over the recitation of "a pair of nucleic acid molecules selected from the group consisting of" because the recited group consists of nucleic acid molecules rather than pairs of nucleic acid molecules.

Claim 52 is indefinite and confusing because it is unclear as to whether the pair consists of any forward and reverse primer set forth in the table or if the pair consists of only specific forward and reverse primers. For example, it is not clear as to whether the claim is limited to pairs that consist of a forward primer of nucleotides 739-757 of SEQ ID NO: 1 and a reverse primer of nucleotides 1941-1924 of SEQ ID NO: 1 or if the claims include a forward primer of nucleotides 739-757 of SEQ ID NO: 1 and a reverse primer of nucleotides 1731-1714 of SEQ ID NO: 1.

Claim 54 and 65 are indefinite because the claims recite a single step of contacting a nucleic acid molecule with a nucleic acid that has been defined in the specification as being useful for determining the H serotype of E. coli. Yet, the claims

require detecting the H and O serotype of E. coli. The claims do not clarify how the detection of the O serotype is accomplished.

Claim 60 is indefinite over the recitation of "the composition of "b," because this phrase lacks proper antecedent basis since claims 58 and 59 do not recite compositions in "b." It is also unclear as to whether "b" includes an additional forward and reverse primer as set forth in claim 60 or if claim 60 is intended to further limit the nucleic acid molecules set forth in "b" of claims 58 and 59. Similarly, claim 61 is indefinite over the recitation of "composition of (a)."

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33 and 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Fields (Journal of Clinical Microbiology. May 1997. 35: 1066-1070).

Fields (see, for example, page 1067 and Figure 1) teaches PCR amplification of the fliC gene of different H serotypes of E. coli, including the serotypes H5, H29, H56, H36, H53, H51, and H44. These nucleic acids have distinct nucleotide sequences and the differences in their nucleotide sequences could be used to distinguish between these H serotypes of E. coli. Accordingly, Fields teaches isolated nucleic acids which encode at least a portion of an E. coli flagellin (fliC) protein, wherein the nucleic acid is

capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Since the H serotypes set forth by Fields are of the same E. coli H types containing the nucleic acids of SEQ ID NO: 7, 28, 54, and 50, it is a property of the nucleic acids of Fields that they contain a least a part of these nucleic acids. Further, Fields (page 1067) teaches 2 nucleic acid primers, one of 25 nucleotides and one of 20 nucleotides (which is considered to be encompassed by "about 10 to 20 nucleotides in length") wherein the primers are capable of identifying an H serotype since the primers can be used to amplify E. coli fliC H serotypes and the amplified nucleic acids can be used to distinguish between the H serotypes. The nucleic acids of Fields contain at least one nucleotide of SEQ ID NO: 13, 56 and 57 and thereby comprise at least a part of SEQ ID NO: 13, 56 and 57. Accordingly, the claimed nucleic acids, primers and compositions are anticipated by Fields.

7. Claims 33 and 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Ratiner (reference 'A6'; Journal of Bacteriology (Feb 1998) 180:979-984).

Ratiner teaches an isolated nucleic acid encoding the E. coli flagellin FIA and flmA genes from serotypes H44, H54 and H55 (see, for example, page 979). These nucleic acids have a distinct nucleotide sequence as compared to the nucleotide sequence of other H serotypes and these differences in the nucleotide sequence could be used to distinguish between these H serotypes of E. coli. Accordingly, Ratiner teaches an isolated nucleic acid which encodes at least a portion of an E. coli flagellin

protein, wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Since the flagellin nucleic acids share some level of sequence identity, the nucleic acids of Ratiner have the property of comprising a least a portion of SEQ ID NO: 1-68. Further, the nucleic acids of Ratiner contain at least one nucleotide of SEQ ID NO: 13, 56 and 57 and thereby comprise at least a part of SEQ ID NO: 13, 56 and 57. Accordingly, the claimed nucleic acids, primers and compositions are anticipated by Fields.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fields in view of Ahren (The Scientist. July 1995. 19 (155): 20-24).

Fields (see, for example, page 1067 and Figure 1) teaches PCR amplification of the fliC gene of different H serotypes of E. coli, including the serotypes H5, H29, H56, H36, H53, H51, and H44. These nucleic acids have distinct nucleotide sequences and the differences in their nucleotide sequences could be used to distinguish between these H serotypes of E. coli. Accordingly, Fields teaches isolated nucleic acids which encode at least a portion of an E. coli flagellin (fliC) protein, wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Since the H serotypes set forth by Fields are of the same E. coli H types containing the nucleic acids of SEQ ID NO: 7, 28, 54, and 50, it is a property of the nucleic acids of Fields that they contain a least a part of these nucleic acids. Further, Fields (page 1067) teaches 2 nucleic acid primers, one of 25 nucleotides and one of 20 nucleotides (which is considered to be encompassed by □about 10 to 20 nucleotides in length□) wherein the primers are capable of identifying an H serotype since the primers can be used to amplify E. coli fliC H serotypes and the amplified nucleic acids can be used to distinguish between the H serotypes. The nucleic acids of Fields contain at least one nucleotide of SEQ ID NO: 13, 56 and 57 and thereby comprise at least a part of SEQ ID NO: 13, 56 and 57. Accordingly, Fields teaches the claimed nucleic acids, primers and compositions.

Fields does not teach packaging the nucleic acids in kits.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, Ahren discloses the general concept of kits for performing nucleic acid detection methods and discloses that kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatibility of the reagents to be used in the assay and allows investigators to save time and money (see for example page 23). Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the nucleic acids of Fields in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art wishing to amplify fliC genes or wishing to use fliC nucleic acids as probes to characterize and detect E. coli H serotypes.

9. Claim 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ratiner in view of Ahren.

Ratiner teaches an isolated nucleic acid encoding the E. coli flagellin FIA and flmA genes from serotypes H44, H54 and H55 (see, for example, page 979). These nucleic acids have a distinct nucleotide sequence as compared to the nucleotide sequence of other H serotypes and these differences in the nucleotide sequence could be used to distinguish between these H serotypes of E. coli. Accordingly, Ratiner teaches an isolated nucleic acid which encodes at least a portion of an E. coli flagellin protein , wherein the nucleic acid is capable of identifying an H serotype of E. coli when hybridized to an E. coli nucleic acid that encodes a flagellin protein and wherein said

nucleic acid does not encode a flagellin protein expressed by E. coli H1, H7, H12, or H48 type strains. Ratiner teaches the use of these nucleic acids to further characterize the E. coli H serotypes. The nucleic acids of Ratiner contain at least one nucleotide of SEQ ID NO: 13, 56 and 57 and thereby comprise at least a part of SEQ ID NO: 13, 56 and 57. Accordingly, the claimed nucleic acids, primers and compositions are anticipated by Fields.

Ratiner does not teach packaging the nucleic acids in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, Ahren discloses the general concept of kits for performing nucleic acid detection methods and discloses that kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatibility of the reagents to be used in the assay and allows investigators to save time and money (see for example page 23). Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the nucleic acids of Ratiner in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art wishing to characterize and detect E. coli H serotypes.

10. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fields in view of Ahren and further in view of Stevenson (reference 'B5'; Journal of Bacteriology. 1994. 176: 4144-4156).

The teachings of Fields and Ahren are presented above. In particular, Fields teaches the analysis of the *fliC* gene and teaches *fliC* nucleic acids. Fields also teaches

that the presently disclosed PCR-RFLP analysis in conjunction with O serotype analysis will be useful in identifying E. coli strains. Fields and Ahren do not teach packaging both *fliC* nucleic acids and nucleic acids encoding a gene for the O antigen in a kit.

However, Stevenson teaches nucleic acids encoding rfb, which is a gene involved in the synthesis of the E. coli O antigen. Stevenson (page 4147 and 4153) also teaches DNA hybridization methods for detecting E. coli O antigens.

In view of the teachings of Stevenson, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included the nucleic acids of Stevenson in the kit containing *fliC* nucleic acids in order to have provided a convenient and cost-effective kit useful for practioners in the art wishing to characterize and detect E. coli H and O serotypes.

11. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ratiner in view of Ahren and further in view of Stevenson (reference □B5'; Journal of Bacteriology. 1994. 176: 4144-4156).

The teachings of Ratiner and Ahren are presented above. In particular, Ratiner teaches flagellin *flA* and *flmA* nucleic acids of E. coli serotypes H44, H54 and H55 and the analysis of these nucleic acids. The combined references do not teach packaging both flagellin nucleic acids and nucleic acids encoding a gene for the O antigen in a kit.

However, Stevenson teaches nucleic acids encoding rfb, which is a gene involved in the synthesis of the E. coli O antigen. Stevenson (page 4147 and 4153) also teaches DNA hybridization methods for detecting E. coli O antigens.

In view of the teachings of Stevenson, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included the nucleic acids of Stevenson in the kit containing flagellin nucleic acids in order to have provided a convenient and cost-effective kit useful for practioners in the art wishing to characterize and detect E. coli H and O serotypes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Carla Myers

November 23, 2004

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER